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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/607,806	06/27/2003	Gail Isabel Reid Adam	SEQ-4032-UT	6270

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EXAMINER	
MARTIN, PAUL C	
ART UNIT	PAPER NUMBER
1655	

DATE MAILED: 03/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/607,806	ADAM ET AL.	
	Examiner	Art Unit	
	Paul C. Martin	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *6-13 and 19-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 14-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 June 2003* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/14/03,11/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-23 are pending in this application.

Election/Restrictions

Applicant's election without traverse of Group I (Claims 1-5 and 14-18) in the reply filed on 12/08/05 is acknowledged.

Claims 6-13 and 19-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/08/05.

The requirement is still deemed proper and is therefore made **FINAL.**

Claims 1-5 and 14-18 were examined on their merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-5 and 14-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In re Wands stated that the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims.

While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The instant specification provides neither working examples or sufficient guidance for how the identification of an interaction between a nucleic acid of indeterminate length or a protein encoded by such a nucleic acid would enable one of ordinary skill in the art to administer an identified compound to a subject in need of fat deposition and obtain results of reduced fat deposition. It is an enormous leap to infer that the presence of an interaction between a test compound and a protein/nucleic acid/etc. allows one to extrapolate such an interaction into a broad effect on a scale up to and including an entire multicellular organism such as a mammal. The invention as claimed would encompass any number of organisms, nucleic acids, proteins and processes involving interactions between them on an scale beyond the reach of the instant disclosure. Certainly, it would involve undue experimentation on the part of the ordinary artisan to make and test these disparate nucleic acids, proteins encoded thereof, and subjects.

Additionally, claims drawn to pharmaceuticals and methods of treatment generally require supporting data because of the unpredictability in biological responses to therapeutic treatments. For the efficacy of a drug treatment *in vivo* faces unfavorable obstacles not present in *in vitro* models. As such, *in vivo* utility necessarily involves unpredictability with respect to physiological activity of an asserted process in humans. See discussion in Ex parte Kranz, 19 USPQ 2d 1216, 1218-1219 (6/90). For examples, drug delivery to the target area must survive the acidic environment of the stomach if administered orally.

Additionally, the delivery of the drug across necessary cell surfaces in amounts needed to be efficacious, but not lethal to the subject, necessitates sensitive testing in order to adequately determine the proper dosage.

Therefore, it is deemed that the claim(s) contains subject matter which was not described in the specification in such a way, as to enable one skilled in the art to which it pertains or with which it is most nearly connected, to make and/or use the invention.

Claims 1-5 and 14-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the production of nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, a nucleotide sequence encoding a polypeptide consisting of the amino acid sequence of SEQ ID NO:2, does not reasonably provide enablement for a nucleotide sequence that is 90% homologous to the amino acid sequence of SEQ ID NO:2 or any fragment of SEQ Ids Nos:1 and 2.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative embodiments.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which can be tolerated in a protein's amino acid sequence and still retain similar biological activity requires a (1) knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e., expectantly intolerant to modification), and (2) detailed knowledge of the ways in which the protein's structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determination to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the real routine of experimentation

One of the main considerations to be made in determining whether undue experimentation is required is the amount of experimentation required. See In re Wands, 8 USPQ2d 1400 (CAFC 1988).

Even if substitutions with natural 20 amino acids encoded by DNA were the only modifications, instant claims would still broadly encompass a multitude of species; calculated as 20^N * (length)!/N/(length-N)! , wherein "20" is the number of natural amino acids encoded by DNA, "N" is the number of positions where substitutions can occur, "!" is the factorial symbol, "/" is the division symbol and "length" is the total number of amino acids in the protein or peptide. A polypeptide chain of 100 amino acids could exist in 10^{130} combinations for example.

While recombinant and mutagenic techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications of other types and the positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar biological activity are limited in any protein/enzyme. The result of such modifications is unpredictable based on the Instant specification. One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g., multiple substitutions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acid modifications in such proteins.

The specification does not support the scope of the claims which encompass all modifications and fragments because the specification does not disclose the following:

a) The general tolerance to modification and extent of such tolerance;

b) The specific positions and regions of the sequence(s) which can be predictably modified and which regions are critical;

c) What fragments can be made which retain the biological activity of the intact protein; and

d) The specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, Applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed protein in a manner reasonably correlated with the scope of the claims, broadly including any number of additions, deletions, or substitutions equaling 90% homology and fragments of any size.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1a and 14a both state "introducing a test molecule to a system which comprises a nucleic acid comprising a PLA2G1B nucleotide sequence...". It is unclear whether it is the test molecule or the system which comprises the nucleic acid comprising a PLA2G1B nucleotide sequence.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3,14 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Lazdunski *et al.* (US 2003/0073087 A1).

Lazdunski *et al.* discloses a method comprising:

a) introducing a test molecule to cells comprising the PLA2G1B nucleotide sequence which encodes a polypeptide of the amino acid sequence of SEQ ID NO:2,

b) determining the presence or absence of an interaction between the test and the polypeptide identifies the test molecule as a Phospholipase A2 inhibitor (Pg. 11, Claim 14 and Pg. 3, Paragraph [0025]).

Lazdunski also teaches a administering a candidate therapeutic identified by the method to a subject for the treatment of disease states or disorders involving Phospholipase A2s, therefore it is inherent in the method of Lazdunski that the method would have the consequence of reducing fat deposition in a subject or treating NIDDM if adminsistered to subjects who happened to be in need thereof.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5,14-16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lazdunski *et al.* (US 2003/0073087 A1) in view of Kazemi *et al.* (WO 02/12562 A2).

The teachings of Lazdunski *et al.* were discussed above.

Lazdunski *et al.* does not teach a method wherein the system is an animal or wherein the PLA2G1B nucleotide sequence comprises a guanine at position 7328, and a thymine at position 9182.

Kazemi *et al.* teaches a method of expressing PLA2G1B in an animal (Pg. 100, Claim 62) and teaches a method wherein the PLA2G1B nucleotide sequence comprises a guanine at position 7328, and a thymine at position 9182 (Pg. 85,Claim 1).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the method of Lazdunski with that of Kazemi because the next logical step in experimentation is to move from testing and screening in cells to higher organisms such as animals. As disclosed by Kazemi, various genotypes of which single nucleotide polymorphisms exist which can alter the expression, structure or function of the target protein or nucleic acid. The ordinary artisan would have been motivated to combine the methods in order to test the technique in higher animals more related systemically then cell culture and with varying single nucleotide polymorphisms (SNP) based on an individual's PLA2G1B haplotype for a more customized treatment.

The ordinary artisan would have had a reasonable expectation of success based on Lazdunski's success in transforming and screening cells for inhibition and Kazemi's demonstration of the importance of SNPs and the use of transformed animals expressing human PLA2G1B as models for disease.

Claim 17 is free of the art.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one with ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence or evidence to the contrary.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Paul Martin
Examiner
Art Unit 1655

02/23/06

PATRICIA LEITH
PRIMARY EXAMINER